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Proline motifs in peptides and their biological processing.

Vanhoof G, Goossens F, De Meester I, Hendriks D, Scharpe S.

Department of Clinical Biochemistry, University of Antwerp, Wilrijk, Belgium.

Many biologically important peptide sequences contain proline. It confers unique conformational constraints on the peptide chain in that the side-chain is cyclized back onto the backbone amide position. Inside an alpha-helix the possibility of making hydrogen bonds to the preceding turn is lost and a kink will be introduced. The conformational restrictions imposed by proline motif in a peptide chain appear to imply important structural or biological function as can be deduced from their often remarkably high degree of conservation a found in many proteins and peptides, especially cytokines, growth factors, G protein-coupled receptors, V3 loops of the HIV envelope glycoprotein gp 120 and neuro- and vasoactive peptides. Only a limited number of peptidases are known to be able to hydrolyze proline adjacent bonds. Their activity is influenced by the isomeric state (cis-trans) as well as the position of proline in the peptide chain. The three proline specific metallo-peptidases (aminopeptidase P, carboxypeptidase P and prolidase) are activated by Mn^{2+} whereas the three serine type peptidases cleaving a post proline bond (prolyl oligopeptidase, dipeptidyl peptidase IV, and prolylcarboxypeptidase) share the sequential order of the catalytic Ser-Asp-His triade, which differentiates them from the chymotrypsin (His-Asp-Ser) and subtilisin (Asp-His-Ser) families. An endo or C terminal Pro-Pro bond and an endo pre-Pro peptide bond possess a high degree of resistance to any mammalian proteolytic enzyme.

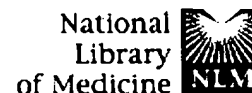
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







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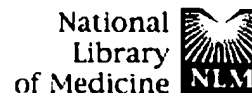
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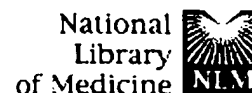
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